

REMARKS

Prior to this amendment, claims 13-20 are pending. By way of this amendment, claims 13, 18, 19 and 20 have been amended. Support for the amended claims can be found throughout the specification and specifically for claim 13 at least in claim 13 as originally filed and page 4 lines 15-20 and page 8 lines 19-20; for claim 18 at least at claim 18 as originally filed; for claim 19 at least at claim 19 as originally filed and page 4 lines 29-30; for claim 20 at least at claim 20 as originally filed and page 4 lines 31-33. After entry of this Amendment, claims 13-20 remain pending.

No new matter has been added. With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any objection and/or rejection made by the Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded claimed subject matter or embodiments in one or more future continuation and/or divisional applications.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 13-20 under 35 U.S.C. §112, first paragraph as allegedly lacking written description. Specifically, the Examiner alleges that the specification has “no showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose.” (OA page 4) The Examiner further alleges that the specification provides “no evidence showing that human STC-1 has no effect on bFGF or VEGF-induced angiogenesis. More importantly, there is no showing that STC-1 inhibits any step of the angiogenesis process of a cell promoted by HGF but not bFGF or VEGF when the cell was exposed to both HGF and bFGF (or VEGF), needless to say any other angiogenic factors.” (OA page 5) Applicants respectfully traverse.

“To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.” MPEP § 2163, I. Applicants note that there is a strong presumption that an adequate written description of the claimed invention exists. (See MPEP § 2163 II (A)) To adequately describe the claims, the specification need not describe *ipsis verbis* what is recited in the claims; rather, the claim limitations may be supported in the specification through implicit or inherent disclosure rather than express disclosure. (MPEP § 2163 I.(B)) Even if the specification does not explicitly recite a claim limitation, sufficient written description exists for the limitation if one of skill in the art can “immediately discern the limitation” from reading the original specification. *Waldemar Link, GmbH & Co. v. Osteonics Corp.*, 31 USPQ2d 1855 (Fed Cir. 1994). Also, “(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent....” (MPEP § 2163.03- citing *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006)).

Applicants have adequate written support throughout the specification for the disclosed method of selectively inhibiting an angiogenic process promoted by a first angiogenic factor but not the angiogenesis process promoted by a second angiogenic factor, comprising administering to a cell exposed to both factors an effective amount of STC-1 (SEQ ID NO: 2) or a variant thereof, wherein the STC-1 or a variant thereof inhibits at least one step of the angiogenic process promoted by the first angiogenic factor but not the second angiogenic factor. As an initial matter, all the limitations of this method are described specifically at least at page 4 lines 10-20 of the instant specification, in claim 13 as originally filed, as well as throughout the specification.

Furthermore, Applicants teach the role of STC-1 as well as the relationship between the disclosed examples of *in vitro* assays and the claimed methods of the invention. So, in addition to teaching the specific words of the claim, and describing STC-1 data in various functional assays throughout the specification and figures, Applicants specifically describe to one of ordinary skill

in the art the correlation of the functional assays to the claimed matter and thus Applicants were in possession of the claimed matter. For Example, Applicants teach “[t]he activities in the Matrigel and migration assay, which are well accepted in the art as models for the multi-staged angiogenesis process, provide unexpected and important evidence for a role for stanniocalcin vascularization and angiogenesis-associated signaling and function.” (Specification page 57 lines 15-18 (emphasis added)). Applicants, in the context of describing the role of stanniocalcin 1 in various stages of angiogenesis, go on to teach that “[t]hese effects were selective to particular angiogenic factors, in particular HGF, because the responses of endothelial cells to either VEGF or bFGF were not modulated in these assays.” (See Specification at page 57 line 19-page 58 line 4) Applicants further describe the role of stanniocalcin 1 in angiogenesis as it relates to the claims in the context of modulation of certain, but not all, steps in the multi-stage angiogenic process generally. Applicants specifically state within that section, “[t]herefore, as described herein, STC-1 provides a unique and potentially highly advantageous target for selective therapeutic modulation of angiogenesis. In one aspect, it is an advantageous target for selective modulation of certain, but not all, steps in the multi-stage angiogenic process.”(Specification at page 58 lines 21-24).

MPEP § 2164.02 states, “[t]he issue of "correlation" is related to the issue of the presence or absence of working examples. "Correlation" as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and a disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention.” Given this standard, one of ordinary skill in the art would have read the specification and found adequate support for a method of STC-1 selectively inhibiting at least one step of an angiogenic process promoted by a first angiogenic factor but not the angiogenesis process promoted by a second angiogenic factor. Furthermore, one of ordinary skill in the art, in the context of the overall teaching of the specification, would have understood the results for each angiogenic factor in

these well known and art-accepted assays, as correlative for the multi-staged angiogenesis process, and descriptive of these factors' effects when administered to a cell exposed to both factors.

Accordingly, one of ordinary skill in the art would have understood from the teachings of the specification, including the claims as originally filed, that Applicants were in possession of the claimed invention at the time of filing, and Applicants submit that claims 1-20, as amended, have adequate written description in the application as filed.

The Examiner also alleges "[t]he instant disclosure of a human STC-1 polypeptide set forth in SEQ ID NO: 2 does not adequately support the scope of the recited genus, which encompasses as substantial variety of homologues or variants of the STC-1 polypeptide of SEQ ID NO: 2." (OA page 6) The Examiner further alleges "The instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the recited genus of STC-1 variants." (OA page 6) Applicants respectfully traverse the rejection.

As an initial matter, while not acquiescing to the rejection, and solely to expedite prosecution, Claim 13 has been amended to include "(SEQ ID NO: 2)".

Applicants clearly teach functional features as well as structural features of STC-1 (SEQ ID NO: 2) or a variant thereof. Applicants provide a definition of "STC-1 polypeptide variants": "a polypeptide having at least one of the biological activities of the STC-1 polypeptides as described herein (including at least an ability to inhibit at least one stage of the multi-stage HGF-induced angiogenic process). . . ." (Specification at page 8 lines 21-24). Applicants teach various assays for relevant functional activity generally throughout the Specification. One such example is a general discussion on methods of screening that includes screening for mimic STC-1 (agonists) or compounds that prevent the effect of STC-1 (antagonists). Included in this discussion is teaching of, for example, structural binding assays,

protein-protein interaction assays, biochemical screening assays, and cell based assays. (See Specification page 36 line 31-page 40 line 9).

More specifically, Applicants teach assays for biological activities of STC-1 polypeptides, including assays for the inhibition of at least one stage of the multi-stage HGF-induced angiogenic process. These assays are described throughout the specification, but Applicants specifically provide examples teaching one of ordinary skill in the art assays for the functional feature that STC-1 inhibits endothelial cell migration. (Specification at page 52 lines 25-32; page 55 line 21-page 56 line 3; Figure 2; page 7 lines 5-15). Also, Applicants provide examples teaching one of ordinary skill in the art assays for the functional feature that STC-1 reduces endothelial cord formation on Matrigel induced by HGF. (Specification at page 52 lines 11-23; page 56 lines 5-13; Figures 3; page 7 lines 16-20). Furthermore, Applicants, as mentioned earlier, go on to teach one skilled in the art that “[t]he Matrigel and migration assay,... are well accepted in the art as models for the multi-staged angiogenesis process...” (Specification at page 57 lines 15-16). Applicants also teach other relevant functional activity assays in which STC-1 and variants thereof could be tested. Examples include but are not limited to descriptions of assays teaching one of ordinary skill in the art assays for STC-1 effects on HGF induced c-met and FAK phosphorylation, and that assays for STC-1 effects on endothelial proliferation. (Specification at page 53 lines 16-24; page 56 lines 15-24; Figure 4; page 7 lines 21-25; page 52 line 34-page 53 line 6; page 55 lines 16-19).

Additionally, Applicants teach one of ordinary skill structural features supporting STC-1 variants throughout the specification. For example, Applicants teach homologues (STC-2) and orthologues (fish) for structural context. (Specification at page 57 lines 4-10; page 59 citations 10 and 11). Applicants teach both how to make anti-STC-1 antibodies and describe specific anti-STC-1 antibodies, and furthermore deposited such antibodies with the ATCC. For example, Applicants teach generally the making of anti-STC-1 antibodies (Specification at least at page 40

line 9-page 49). More specifically Applicants describe the preparation and deposit of specific monoclonal antibodies to STC-1. (Specification at least page 50 line 24-page 51 line 14).

These deposited antibodies bind to specific structural elements on STC-1. Applicants go on to teach the activity of one or more deposited anti-STC-1 antibodies in various functional and structural assays also described by Applicants, including the previously mentioned endothelial cell migration assay. Applicants also teach an ELISA assay as well as a western blotting assay for STC-1. (Specification at least page 51 lines 16-27; page 52 lines 4-9).

"If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." (MPEP § 2163 II.A.3(a)).

Furthermore, "[t]he 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge.... As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution (citation omitted)." (MPEP § 2163 II.A.3(a)) Given the state of the art at the time of the invention one of ordinary skill would find the instant disclosure of a human STC-1 polypeptide set forth in SEQ ID NO:2 and the teaching of the instant Specification provides adequate teaching to identify and be in possession of STC-1 variants. In light of the foregoing standards, the present claims are clearly adequately described by the specification. Accordingly, one of ordinary skill in the art would have understood from the teachings of the specification that Applicants were in possession of the claimed invention at the time of filing, and Applicants submit that claims 1-20, as amended, have adequate written description in the application as filed. Applicants respectfully request that the rejection of claims 13-20 under 35 U.S.C. §112, first paragraph written description be reconsidered and withdrawn.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 13-20 under 35 U.S.C. §112, second paragraph, as allegedly “indefinite because they recite “STC-1”. Such term is determined arbitrary and may change with time.” (OA page 7 paragraph 7).

While not acquiescing to the rejection, and solely to expedite prosecution, claim 13 has been amended. Independent claim 13 has been amended to include “ (SEQ ID NO: 2)” rendering the instant rejection moot.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, second paragraph.

Claim Objections—Minor Informalities

The Examiner has objected to claims 13, 19 and 20, stating: “(i). claim 13 is being objected to because the word “and” in line 2 between “a first angiogenic factor” and “but not” is not needed” and “(ii). Claim 20 [as well as claim 19]... under 37 CFR 1.75 (c), as being of improper form for failing to further limit the subject matter of a previous claim.” The Examiner notes that claim 20, as well as 19, “recites “wherein STC [sic] or variant thereof does not *substantially inhibit*...”. (OA page 7-8 paragraph 8) Applicants respectfully note that the claims recite “STC-1” not “STC”.

Applicants, while not acquiescing to the objection, and solely to expedite prosecution, have amended independent claim 13 to remove “and”, rendering part (i) of the instant objection moot. Furthermore, while not acquiescing to the rejection, and solely to expedite prosecution, claims 19 and 20 have been amended removing “substantially”, rendering the part (ii) of the instant objection moot.

Applicants respectfully request that the Examiner reconsider and withdraw the objections.

CONCLUSION

Applicants believe that the pending claims are in condition for allowance, and respectfully request that a timely Notice of Allowance be issued in this case. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is **strongly encouraged** to call the undersigned at the number indicated below.

Applicants respectfully request entry of these amendments and prosecution on the merits. Please grant any extensions of time and charge any required additional fees to Deposit Account No. 07-0630. The Examiner is invited to contact the undersigned at (650) 225-5733 if any issues may be resolved in that manner.

Respectfully submitted,
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